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A CASE OF YEAST (MONILIA) INFECTION OF THE LUNG.

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THROUGH the courtesy of Dr. A. C. Harrison, of Baltimore, I was recently enabled to study a case of yeast infection of the lung which is sufficiently interesting from various points of view as to warrant its publication.

CASE HISTORY. The patient, J. E. S., male, aged about thirty years, an employee of a gas company, was sent to Dr. Harrison for examination, as his health had evidently been failing for about a year. While his normal weight was 148 pounds he now weighed only about 130 pounds. He complained of becoming tired very easily, had had occasional night sweats, and cough and expectoration. He would periodically feel quite normal, however, but his cough and expectoration would then return and again persist for a variable time. The patient's appetite had not suffered; there was no diarrhea and no history of ulceration of the skin.

With the idea in mind that he might possibly be suffering from tuberculosis, Dr. Harrison sent a specimen of the patient's sputum to me for examination. This was slightly mucopurulent and free from tubercle bacilli, but crowded with yeast cells occurring either singly or in budding form. This observation was so surprising that another specimen of sputum was secured under conditions which excluded every possible chance of accidental contamination. The finding in this was the same: there were no tubercle bacilli but innumerable yeast cells. The conclusion was accordingly that the patient was most likely suffering from a yeast infection of the lung.

As the physical examination revealed nothing abnormal, in particular no rales, no dulness, and no impairment of the breath sounds, a fluoroscopic examination was made by Dr. H. E. Ashbury, who reported as follows:

"The movements of the diaphragm are equal on both sides. There is some thickening of the bronchi leading to the upper lobes. Stereoscopic pictures show a diffuse infiltration about the hilum of both lungs, extending upward to both upper lobes and involving the right middle and lower lobes. The bases are only very slightly

involved. The appearance is that of tuberculosis, showing the interweaving of the bronchial markings with some studding of small calcified bodies, giving the appearance of mottling. Much of the thickening above the hila is due to glandular enlargement. The cardiovascular shadow is normal, and gives no evidence of involvement of the mediastinal glands."

The examination of the blood showed the following: Wassermann negative. Hemoglobin, 88. Red count, 4,664,000. Color index, 0.94. White count, 6500, of which 41 per cent. were small mononuclears, 5.3 per cent. large mononuclears, 51.3 per cent. polynuclear neutrophils, 1.3 per cent. eosinophils, and 1 per cent. basophils.

The urine contained neither albumin, sugar, diacetic acid, nor acetone, and showed no increase of indican. Microscopically there was nothing unusual.

Examination of the feces revealed a few small oval, budding yeast cells, such as may be found in any specimen. Their cultivation (in a single attempt) was not accomplished.

Scrapings from the tongue showed no yeast cells. From the sputum the organism in question was readily obtained in pure culture, and has now been under observation for twelve months.

In the sputum the organism occurred in torular form only. The individual cells were nearly round, the majority occurred singly, and only occasional ones were budding. Their size was fairly uniform, averaging 6μ . Viewed with the oil-immersion lense each cell showed a round highly refractive little body, measuring from 1 to 2μ in diameter and smaller granules. Some of the cells appeared vacuolated, and with a certain focus their outline was doubly contoured. Unstained, the cells had a greenish shimmer. Treated with Lugol's solution the torular cells assumed a faint yellowish color. With the usual methods of staining no very satisfactory differentiation of the cell contents could be obtained, as it was difficult to avoid overstaining. With a very dilute solution of safranin, however, the nucleus could be brought out in most of the cells. Spores were not observed, nor were mycelial threads seen in the sputum.

In cultures, cells were occasionally seen which carried a daughter cell of almost equal size as the mother cell, from which in turn an elongated cell was given off, and from this a short row of smaller oval cells. At the same time cells were occasionally encountered which appeared sausage shaped, measuring 12 to 13μ in length by 2.5μ in breadth.

Cultures on agar grew out abundantly in twenty-four hours, and were of a white, creamy appearance and consistence. In these the organism still retained its torular form, with occasional premycelial types, the latter especially in cultures that had grown for a week or longer. But even after transplanting for twelve

months, at weekly intervals, the torular form predominates by far. Generally speaking the cells were for the most part smaller in the cultures than in the sputum, measuring from 3 to 6 μ in diameter, but much larger specimens were also quite common, and these usually oval, measuring 7 by 11 μ . In the cultures all the cells appeared provided with a large vacuole, which almost filled the body of the organism, and lying on top or within it a small highly refractive body.

In the young cultures most of the cells showed no buds at all; some were provided with a single bud, none with more. Several buds were only observed in old broth cultures.

On Petroff medium, containing gentian violet, a comparatively restricted growth occurred, in which numerous premycelial forms were noted.

In anaërobie stab cultures under oil, growth occurred along the line of the stab, and radiating out from this, as a central axis, large numbers of fine hair-like filaments penetrated the solid agar, so that at the expiration of about six weeks the appearance was that of a fine bushy tail in the substance of the agar. The growth first appeared while the tube was kept at incubator temperature, but later it developed at that of the room and showed a certain degree of heliotropism. Immediately under the oil a moderately dense mycelium developed with abundant lateral production of conidia. Frozen sections cut at right angles to the long axis of the cylinder of agar showed that the hair-like processes represent single mycelial threads with terminal as well as lateral bunches of conidia.

Chlamydospore-like terminal formations were occasionally encountered in the anaërobie cultures as well as on Petroff's medium.

True ascospore formation was not observed.

The hyphal threads of the mycelium were segmented.

A production of aerial hyphae was not noted during the twelve months of observation. In plain bouillon the organism develops fairly readily, forming a granular-looking sediment while the supernatant fluid remains clear.

In liquid white of egg (alkaline) a similar growth is obtained, though it is somewhat less abundant.

Its behavior in litmus milk is especially striking. There is apparently no change during the first week or ten days, above all no acid production. After a longer period, however, there appears to be an increase in the alkalinity of the medium, while at the same time coagulation occurs; this state persists without subsequent digestion taking place.

Glucose bouillon is slightly fermented after twenty-four hours; in the next twenty-four hours this increases a little, but after that it seems to cease. Lactose, saccharose, inulin, and mannite are not fermented.

The organism is markedly pathogenic for rabbits. One animal

which had been given 5 c.c. of a bouillon culture intravenously at 11 A.M., January 17, was rendered quite ill, and was found dying early in the afternoon of January 20. At the autopsy, which was made immediately after killing the animal with chloroform, most extensive macroscopic lesions were found in both kidneys, which were studded with innumerable white nodules of pin-point size. These were confined to the cortex.

Equally striking was the appearance of the appendix. This was likewise studded with miliary nodules, which did not extend, however, macroscopically beyond the line of junction with the cecum. Microscopically, the lesions in question were essentially areas of necrosis, surrounded and partly infiltrated with leukocytes. Microscopically there was in addition the picture of an acute diffuse nephritis. In the appendicular and renal lesions the offending organism was found practically exclusively in mycelial form, while in the urine in addition to this the torular type was present in enormous numbers. In the lungs there were no lesions which were comparable to those in the kidneys and the appendix. Instead there were numerous hemorrhagic areas containing large numbers of the organism in torular form, but no evidence of mycelial production.

At the time of writing the organism has almost lost its tendency to produce mycelial forms even under anaërobic conditions, but is still pathogenic.

As regards the subsequent history of the patient I can add that following the administration of potassium iodide in full doses the cough and expectoration ceased, and that he has not only regained his former weight but has even added thereto. Apparently he is well, but whether *post hoc* or *propter hoc*, and whether or not the improvement will be lasting, it is of course impossible to say at present.

As regards the botanical position of our organism my feeling is that our present knowledge of the group of which it evidently is a member is as yet too meager to warrant any dogmatic statements. Its general biological characteristics are essentially the same as those of the organism which Bahr¹ and Ashford² regard as the cause of sprue, and which these writers view as monilia.

When I first discovered the organism in the sputum I was under the impression that the case was an instance of blastomycosis of the lung, but its smaller size, its disinclination to mycelial formation, its non-production of aerial hyphæ, and its marked pathogenic properties seemed to rule this out.³ The absence of endosporulation and the very evident tendency to multiply by budding, on the other hand, distinguished it from the *Coccidioides immitis* of California.⁴

¹ Tr. Soc. Trop. Med. and Hyg., April, 1914, xi, No. 5.

² Am. Jour. Med. Sc., 1915, cl, 680.

³ Stöber: Arch. Int. Med., 1914, xiii, 509.

⁴ Ibid., 1915, xv, 608.

The only other instance of monilia infection of the lung which has thus far been recorded is that of Boggs and Pincoff.⁵ Their organism, it is true, gradually developed a tendency to mycelial formation, but its behavior in other respects is so similar to my own that I am inclined to regard the two as identical. Morphologically, theirs as well as my own are indistinguishable from that of Bahr and Ashford, but the evident affinity of the latter for the intestinal tract in the human being, and of Boggs and Pincoff's and my organism for the lung, would, for the present at least, warrant the separation of the two types, which might appropriately be termed *monilia intestinalis* and *monilia pulmonalis* respectively.

THE ROLE OF THE LEUKOCYTES IN VIRIDANS ENDOCARDITIS AND THE EFFECT OF NUCLEIN INJECTIONS.

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THE work of the past ten years tends to lay more importance on the vital activity of the white-blood cells and their enzymes than was accredited to them during the period of enthusiastic adoption of the humoral theories. While the hopes raised by the work of Petterson, Hiss, Zinsser and others that leukocytic injections would enhance resistance in various diseases have not been fulfilled, these investigations have served the purpose of bringing out the true value of intraphagocytic and extraphagocytic bacterial destruction and the balancing of enzyme and antienzyme. The behavior of leukocytes in frank pyogenic affectings is fairly well understood, but in the more chronic diseases, and those with less activity of the leukocyte-producing tissue, the subject is far from clear. The value of the leukocytes as a defense in typhoid has only lately received any approximately acceptable estimation, and in tuberculosis we know practically nothing about it. In no condition would a thorough understanding of leukocytic defensive activity be more helpful than in subacute endocarditis, a pathogenic process whose inception and continuation imply a high degree of adaption of invaders to defenses. It was with the hope of learning something

⁵ Johns Hopkins Hosp. Bull., 1915, xxvi, 407.